The frequency of a segregating duplicate gene

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Duplicate genes

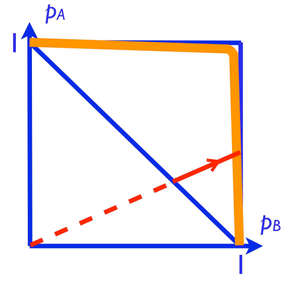
Sometimes, the process of reproduction results in genes which are not only mis-copied (mutations) but which are copied into the wrong place in the genome. This produces a *duplicate* gene. Genome projects have revealed multitudes of duplicated genes across a wide variety of species. The existence of duplicate genes is thought to be critical in the process of genetic innovation: duplicates are free to explore new variations, perhaps finding advantageous new forms, without depriving the organism of any essential functions performed by the original gene. Knowing the population genetics of a duplicate, i.e. the way in which a duplicate can spread through a population, is an essential step towards a quantitative understanding of how this evolution can proceed.

Loosely-linked models

Take a haploid model which allows for recombination: that is, with probability r an offspring takes genes at original and duplicate loci from different parents.

A and B represent functional alleles at the original and duplicate loci; N and O are mutated, non-functional versions of the gene (these mutations are assumed to occur with probability u at each reproduction event; an NO individual is not viable).

Eventually, all individuals will be AO (*duplicate loss*) or all individuals will be NB (*map change*). Although the state of the process is described by p_A and p_B, simulations show that the process remains largely in a mutation-selection balance described by a hyperbola in (p_A, p_B)-space.



Diffusion modelling implies the hyperbola is approached along lines through the origin. As a result the process will be analyzed via a one-dimensional diffusion. The diffusion variable will be taken as $g = p_B/(p_A+p_B)$.

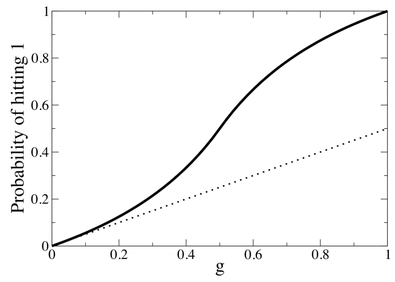
WATTERSON (1983) used a similar approach but with a "fast" diffusion around and a "slow" diffusion along the hyperbola.

The one-dimensional diffusion

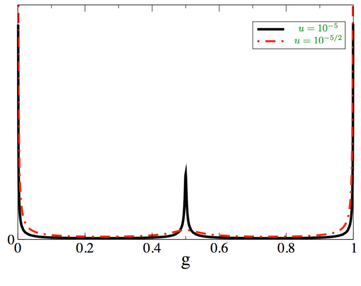
The one-dimensional diffusion along the hyperbola has infinitesimal mean and variance

$$\frac{2-\varepsilon}{2}(2g-1)g(1-g)$$
$$\frac{g(1-g)}{2}\left(1-2(2-\varepsilon)g(1-g)+\sqrt{1-2(2-\varepsilon)g(1-g)}\right).$$

Here ε is a composite parameter roughly equal to the mutation rate. More meaningfully, this diffusion has scale function and speed densities as illustrated below:



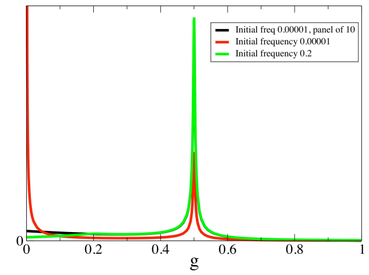
Scale function: for small initial duplicate frequencies g_0, the probability of map change is $g_0/2$.



Speed density: there is the usual slow-down near absorbing points, but also near equi-frequency, indicating that a duplication process not on the verge of map change or loss of the duplicate is likely to be very close to equi-frequency.

Observed frequencies

As the speed density does not correspond to a probability distribution, it doesn't provide direct information about what frequency an active or *segregating* duplication is likely to be observed at. For this kind of information there is the pseudo-transient distribution (EWENS 1963).



This is a probability distribution for the time spent at a certain frequency before loss or map change. Note that:

- there is a local peak at the initial frequency
- for small initial frequencies the spike in the middle gets smaller: most of the duplicates seen are newly-arisen and being quickly lost

However, a duplicate that is quickly lost is unlikely to be identified in a population without considerable sampling effort. This is *ascertainment*: one might find duplicates by examining a small number of individuals (called a panel), but then determine their frequencies by examining a larger sample or even the whole population. Doing this, we see that the spike at $g = 0.5$ increases again – although there is still a slightly greater tendency to pick up low frequency duplicates.

The intuitive reason for the spike is that evolution proceeds slowly near $p_A = p_B = 1$ since there is little genetic diversity: most change comes from mutation which is assumed to be rare.

References

EWENS, W.J. (1963). The diffusion equation and a pseudo-distribution in genetics. *Journal of the Royal Statistical Society. Series B (Methodological)* **25** 405–412.

WATTERSON, G. A. (1983). On the time for gene silencing at duplicate loci. *Genetics*. **105** 745–766.